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: Unknown
: Herewith

Please replace the word "expiration" with --expression vector-- found on page 16, line 2.

Please replace the words "The pups will usually be..." with --Offspring are generally...--
found on page 20, line 17.

Please insert the word --are-- on page 22, line 12 after the word "Preferred."

Please insert the word --that-- on page 22, line 14 after the word "lines."

Please delete the paragraph beginning at page 26, line 7.

IN THE CLAIMS:

Please cancel the following claims: 2, 9, 10, 11, 12, 16, 19, 21

Please amend the remaining claims as follows:

1. (Amended) An isolated or purified polynucleotide encoding a mutant mouse parkin2 protein, or a homolog thereof, wherein said mutant causes symptoms of Parkinson's disease.

3. (Amended) The polynucleotide of claim 1, wherein said polynucleotide is selected from the group consisting of: SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO: 9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, and SEQ ID NO:20.

4. (Amended) A vector, comprising the polynucleotide of claim 1.

5. (Amended) A cell, comprising the polynucleotide of claim 1.

6. (Amended) The cell of claim 5, wherein the cell is a prokaryotic or a eukaryotic cell.

7. (Amended) A parkin mouse protein, comprising any amino acid sequence selected from the group consisting of: SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, and SEQ ID NO:34.

8. (Amended) A transgenic non-human mammal comprising the isolated or purified polynucleotide of claim 1.

13. (Amended) A mammalian cell-line transformed or transfected with the polynucleotide of claim 1.

14. (Amended) A method of producing a transgenic animal, comprising:

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constructing a vector that carries the polynucleotide of claim 1;
introducing said vector into embryonic stem cells;
injecting said embryonic stem cells into blastocysts; and
placing said blastocysts into a pseudopregnant female animal.

15. (Amended) A mammalian model for a neurodegenerative disease comprising the transgenic mammal of claim 8.

17. (Amended) A method for testing the efficacy of a treatment for a neurodegenerative disease, comprising:

subjecting the mammalian model of claim 15 to a putative treatment or agent; and
determining the efficacy of said treatment by identifying a reduction in the symptoms of said neurodegenerative disease.

18. (Amended) The method of claim 17, wherein said neurodegenerative disease is selected from the group consisting of: Parkinson's disease, Alzheimer's disease, Huntington's disease, amyotrophic lateral sclerosis, Multisystem atrophy, Wilson's disease, Pick's disease, and Prion disease.

20. (Amended) A method for testing whether an active substance is useful for treating the symptoms of Parkinson's disease comprising:

administering said active substance to the transgenic animal of claim 8; and
determining whether said active substance reduces the symptoms of Parkinson's disease.

22. (Amended) A descendant of the transgenic animal according to claim 8, wherein said animal is obtained by breeding with the same or any other genotype.

Please add the following claims:

23. (New) The polynucleotide of claim 1, wherein said mutant comprises a point mutation, deletion or fragment.

24. (New) The polynucleotide of claim 1, wherein said homolog is human.

25. (New) The cell of claim 5, wherein said eukaryotic cell is a fungal, insect or mammalian cell.

26. (New) The cell of claim 25, wherein said fungal cell is a yeast cell.

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27. (New) The cell of claim 25, wherein said prokaryotic cell is a bacterial cell.

28. (New) The polynucleotide of claim 1, wherein said mutants comprise mutations in exon 1 or exon 3.

29. (New) The ~~mammalian~~ model of claim 15, wherein said animal is a mouse or rat.

30. (New) A method of testing agents for efficacy and toxicity in treating a neurodegenerative disease, comprising:

administering said agent to the mammalian model of claim 15; and

identifying whether said agent reduces the symptoms of said neurodegenerative disease or is toxic to said mammal.

31. (New) A method for testing whether an active substance is useful for treating the symptoms of Parkinson's disease, comprising:

administering said active substance to the cell-line of claim 13; and

determining whether said active substance reduces the symptoms of Parkinson's disease.

32. (New) The method of claim 20, further comprising testing various dosages of said active substance.

REMARKS

The foregoing amendments more closely conform the application to U.S. practice. The above requested changes to the application do not add new matter, and entry of the amendments is respectfully requested.

The specific changes to the specification are shown on a separate set of pages attached hereto and entitled VERSION WITH MARKINGS TO SHOW CHANGES MADE, which follows the signature page of this amendment. On this set of pages, the insertions are underlined while [brackets denote deletions].

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410. A duplicate copy of this sheet is enclosed.

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Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 4/26/01

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